

Amendments to the Specification:

Please replace the original paper copy of the Sequence Listing with the substitute paper copy of the Sequence Listing filed herewith.

At page 1, line 1, please delete subheading:

~~DESCRIPTION~~

Please insert the following new paragraph after the title:

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is the National Stage of International Application No. PCT/JP2004/010444, filed July 15, 2004, which claims the benefit of United States Patent Application Serial No. 60/487,333, filed on July 15, 2003. The contents of both applications are hereby incorporated by reference in their entireties.

Please amend the paragraph beginning at page 9, line 3, as follows:

~~The host cell from which the transformed cell of the present invention can be obtained and methods for transforming the cell are described in detail below.~~ First, DNA encoding the desired H and L chains is incorporated into an expression vector. Another gene encoding the J chain may be combined with the DNA for incorporation into the expression vector. These genes are incorporated into the expression vector so that they will be expressed under the control of expressional regulatory regions.

Please amend the paragraph beginning at page 14, line 8, as follows:

When using a eukaryotic cell, for example, an animal, plant, or fungal cell may be used as the host cell. As an animal cell line or a human cell line, the mammalian cell lines listed below are known, for example.

- CHO (hamster ovarian cell, J. Exp. Med. (1995) 108, 945),

- COS (monkey kidney cell, Miyazaki, *et al.*, Gene (1989) 79, 269),
- 3T3 (mouse fibroblast),
- PC12 (human plasmacytoma, Neumann, *et al.*, EMBO J. (1982) 1, 841),
- BHK (baby hamster kidney),
- HeLa (human epithelial cell, Cattaneo, *et al.* EMBO J. (1987) 6, 2753),
- C6 (human glioma cell, Cattaneo, *et al.* Eur. J. Biochem. (1983) 135, 285)□
- Vero (monkey kidney cell, Cytology (1991) 7, 165), and
- Amphibian cells such as *Xenopus* oocyte (Valle, *et al.*, Nature (1981) 291, 358-340).

Please amend the paragraph beginning at page 17, line 3, as follows:

The animal cells, such as CHO cells, transformed with the IgM expression vector secrete IgM into the culture supernatant. Accordingly, the culture supernatant may be collected to obtain the target IgM. IgM can be purified from the culture supernatant by a purification technique including gel filtration, ion exchange chromatography, and affinity chromatography (Antibodies: A Laboratory Manual. Ed Harlow and David Lane, Cold Spring Harbor Laboratory, 1988). The present invention provides a method for manufacturing a substantially pure IgM purified from the culture supernatant. As used herein, the term “substantially pure IgM” can be defined as IgM free from any other proteins derived from transformed cells and culture media of the biological species from which the IgM molecule is derived. For example, when the IgM molecules collected from the cell transformed with the human-derived IgM gene are free from any proteins other than the human-derived IgM protein, this IgM can be referred to as substantially pure IgM. ~~In the case of mouse-human chimeric IgM, an IgM free from any other mouse proteins or human proteins is a substantially pure IgM.~~ Herein, it is preferable that the substantially pure IgM be substantially free from any other proteins derived from host cells or protein components of the culture solution used for culturing the host cells. The term “substantially free” means that the percentage of other protein components to total proteins is 20% or less, for example, 10% or less, preferably 5% or less, or 2% or less, and more preferably 1% or less.

Please amend the paragraph beginning at page 24, line 25, as follows:

FIG. 5 shows the measured cytotoxic activity of recombinant L612. The upper panel shows the results obtained using addition of whole blood as a complement source, and the lower panel shows the results obtained using addition of undiluted human-derived plasma as a complement source. The vertical axis indicates the percentage (%) of specific $^{51}\text{Cr}[[\text{C}]]$ release by target cells. The horizontal axis shows the concentration of the antibody ($\mu\text{g/mL}$).

Please amend the Table 3, on page 40, as follows:

Table 3

	J chain	aggregate	hexamer	pentamer	tetramer
L612 (<u>native</u>)	+/-	5%	18%	73%	3%
CA19 (<u>recombinant L612</u>)	-	5%	82%	10%	3%
CJ45 (<u>recombinant L612</u>)	+	4%	6%	90%	-

Please amend the paragraph beginning at page 45, line 35, as follows:

Using the culture supernatant obtained by culturing the cell lines obtained by Geneticin selection for three days with an initial cell density of 2×10^5 cells/mL in an S100 spinner flask, non-reducing SDS-PAGE was conducted according to the method described in Example 3, and Western blot was performed using anti-human μ chain antibody as the primary antibody. As a result, a band corresponding to the L612 pentamer obtained mainly from L612-expressing B cells was obtained for the pL612pentaCA4 transformed cell lines, but a band corresponding to the hexamer was not detected (Fig. 4). It was demonstrated that, by placing the J chain expression unit with the H and L chain expression units on a single expression vector and appropriately controlling the expression level of the J chain relative to those of the H and L chains, the pentamer L612 could be mainly produced.